REMARKS

The Rejection of Claims 14-23 Under 35 U.S.C. §112, first paragraph

Claims 14-23 are rejected as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors at the time the application was filed had possession of the claimed invention. The Office Action states that the claims recite antisense molecules that are "tartgeted to gene sequences, mutated sequences, allelic variants, splice variants, sequences that have a recited degree of identity (similarity, homology), and so forth." This statement does not appear to accurately describe the claims. For example, no degree of identity is recited, nor are any mutated sequences, allelic variants, or splice variants recited. Applicants have amended the claims to recite the sequence of 14-3-3σ. However, sequences could be targeted that are allelic variants or mutated without departing from the spirit of the invention. Any 14-3-3σ gene could be targeted to which such antisense molecules bind.

Withdrawal of the rejection is requested in view of the amendment to all independent claims.

The Rejection of Claims 20-23 Under 35 U.S.C. §112, first paragraph

Claims 20-23 are rejected as failing to comply with the enablement requirement. Claims 20-23 were said to embrace methods of antisense based therapy. The basis of the rejection is that therapy of whole animals with antisense is unpredictable. Claims 20-23 have been amended to recite administration to cells in culture. As the treatment of whole animals is no longer encompassed by the claims as amended, this rejection is no longer appropriate for the claims.

Applicants enclose a copy of an article by Dellambra *et al., Journal of Cell Biology, 149:*1117-1129 (2000) which demonstrates the biological effect of 14-3-3σ antisense on cells in culture. Indeed, the antisense causes the cells to bypass senescence and maintain telomerase activity.

Withdrawal of the rejection is respectfully requested.

The Rejection of Claims 14 and 15 Under 35 U.S.C. §103(a)

Claims 14 and 15 are rejected as unpatentable over Prasad, Weintraub, and James. This rejection is respectfully traversed.

Claims 14 and 15 are directed to an antisense construct comprising a transcriptional promoter, a transcriptional terminator, and a segment of 14-3-3σ which is complementary to 14-3-3σ mRNA.

Prasad is cited as teaching the 14-3-3σ nucleic acid sequence and that its expression is associated with cancer. Prasad does not teach the biological function of the encoded protein. Weintraub is cited as teaching that antisense methods can be used to determine biological function of genes. James is cited as teaching promoters, terminators, and inducible promoters. The PTO asserts that it would have been *prima facie* obvious to make the claimed antisense constructs, combining the teachings of the references. The PTO asserts that one of skill in the art would have been motivated to make the claimed antisense constructs in order to determine the function of Prasad's nucleic acid sequence.

The rejection overstates Weintraub's actual teaching. While Weintraub provides examples of "contributions" that antisense methods have made to understanding gene function, he does not teach that this is a general method that will be applicable to or fruitful with any gene. Weintraub teaches the use of antisense with three transforming oncogenes (*fos*, *ras*, and cyclin). Page 45. There is no suggestion to use this method on sigma in particular, or on any other genes. Thus, there is no suggestion to combine Weintraub's technique with Prasad's gene.

A *prima facie* case of obviousness fails if it is based on an "obvious to try" standard.

> An "obvious-to-try" situation exists when a general disclosure may pique the scientist's curiosity, such that further investigation might be done as a result of the disclosure, but the disclosure itself does not contain a sufficient teaching of how to obtain the desired result, or that the claimed result would be obtained if certain directions were pursued.

In re Eli Lilly & Co., 14 U.S.P.Q. 1741, 1743 (Fed. Cir. 1990).

The PTO merely outlines a research project—determining the biological function of the gene—with a general approach to solve it. Making an antisense molecule, as taught by Weintraub, is only a technique which might give clues to biological function. However, this is merely a direction of research to follow, with no indication of what the final result would be, or if it would be achieved.

Examination of the PTO's asserted motivation for combining the references ("to determine the function of HME1 since Prasad et al have taught that HME1 expression is associated with cancer") reveals that the asserted motivation is a purely academic or philosophical goal leading to no particular practical result. While this may be sufficient motivation to undertake an academic plan of research, this is not a sufficient motivation according to the patent law. The Court of Customs and Patent Appeals in *In re Stemniski* denigrates "abstract, theoretical, or academic considerations." 170 U.S.P.Q. (BNA) 343, 347 (C.C.P.A. 1971). The court looked to

> practical considerations which promote the progress of the useful arts or are of use to society . . . . Where the prior art reference neither discloses nor suggests a utility for certain described compounds, why should it be said that a reference makes obvious to one of ordinary skill in the art an isomer, homolog or analog of related structure, when that mythical, but intensely practical, person knows of no "practical" reason to make the reference compounds, much less any structurally related compounds?

The motivation asserted by the PTO is merely to study and possibly uncover a protein's mechanism of action. This is not the type of motivation that the courts have imbued in the "that mythical, but intensely practical, person," the one of ordinary skill in the art.

The *prima facie* case of obviousness fails because the asserted motivation to combine the references relies on a theoretical and abstract philosophical inquiry. Prasad taught that cancer cells expressed less HME1 than normal cells. Determining

the mechanism of action of the protein would not have been viewed by the ordinary artisan as promoting any practical goal.

Withdrawal of the rejection is therefore requested.

The Rejection Of Claims 16-18 and 19 Under 35 U.S.C. §103(a)

Claims 16-18 and 19 are rejected over two combinations of references, each of which relies on Prasad and Weintraub. Claims 16-18 are additionally rejected in view of Baracchini, and claim 19 is additional rejected over Baracchini in view of Prakash.

Baracchini is cited as teaching antisense oligonucleotides and modifications to their backbones. Prakash is cited as teaching circular antisense constructs. Neither of these two references remedies the deficiency of the primary references in forming a *prima facie* case. Neither of these two references provides any practical, real-world motivation to make the recited construct. Each of these rejections relies on the motivation of determining the gene function. Many different experiments can be proposed to try to determine a gene's function. There is no direct and unambiguous route to this goal. The route is one of trial-and-error experimentation. The claimed molecules would not have been obvious, as the standard is defined by the courts, over the cited prior art.

Respectfully submitted,

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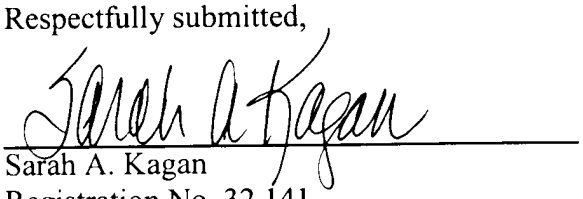
By: 

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